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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,418	06/08/2000	MAMORU HORIKOSHI	Q58140	1158

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SUGHRUE MION ZINN
MACPEAK & SEAS
2100 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20037

EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,418	HORIKOSHI ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 8* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 10, 2003, has been entered.

[2] Claims 1-2, 5, and 8 are pending in the application.

[3] Applicants' amendment to the claims filed September 10, 2003 is acknowledged. This listing of the claims replaces all prior versions.

[4] Applicant's arguments filed in the amendment of September 10, 2003 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

[6] The indicated allowability of claim 2 is withdrawn upon reconsideration of the claim for those reasons stated below.

Claim Rejections - 35 USC § 112, First Paragraph

[7] Claims 1, 2, and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 (claim 8 dependent therefrom) is drawn to (in relevant part) a genus of isolated mutant protophorphyringogen oxidase (protox) polypeptides that are naturally occurring in *N. tabacum*, having enzyme activity equivalent to SEQ ID NO:2, and having tolerance to photobleaching herbicide equivalent to SEQ ID NO:2. Claim 2 is drawn to the polypeptide of claim 1, comprising a genus of polypeptides having one or more deletions of SEQ ID NO:2.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the genus of mutant naturally

occurring *N. tabucum* protox polypeptides is described only by function as the specification fails to disclose the structure of even a single representative species of the genus of claimed mutant protox polypeptides. As such, the specification fails to provide a sufficient description of the claimed genus of protox proteins as the specification merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus. The CAFC in *UC California v. Eli Lilly*, (43 USPQ2d 1398) stated that: "In claims to genetic material, however a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA", without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus". Similarly with the claimed genus of protox proteins, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus. Given the lack of description of a representative number of species, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

Applicants traverse the instant rejection arguing that claim 1 has been amended to limit the mutant protox polypeptides to those that are naturally occurring in *N. tabacum*, have the enzyme activity of SEQ ID NO:2, and have tolerance to photobleaching herbicide equivalent to SEQ ID NO:2. Applicants argue that because the claimed mutant protox polypeptides occur in the same organism, i.e., *N. tabacum*, the representative species supports the claimed genus. Applicants' argument is not found persuasive.

It is noted that the examiner can find no disclosure of even a single representative example of a mutant protox polypeptide as encompassed by the claims. Applicants are invited to demonstrate that such a mutant protox polypeptide has been disclosed. However, even if the specification disclosed a single representative species, this disclosure would fail to describe the entire genus of claimed mutant protox polypeptides as the genus encompasses species having widely variant structures that cannot be predicted *a priori* and MPEP § 2163 states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus".

[8] Claims 1, 2, and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated polypeptide of SEQ ID NO:2, does not reasonably provide enablement for *all* isolated mutant protophorphyringogen oxidase (protox) polypeptides that are naturally occurring in *N. tabacum*, having enzyme activity equivalent to SEQ ID NO:2, and having tolerance to photobleaching herbicide equivalent to SEQ ID NO:2 (claim 1) and optionally having one or more deletions of

SEQ ID NO:2 that maintain protox activity and tolerance to photobleaching herbicide (claim 2). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass *all* isolated naturally occurring *N. tabacum* mutant protophorphyringogen oxidase (protox) polypeptides as encompassed by the claims. The broad scope of the claimed polypeptides is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mutant protox polypeptides broadly encompassed by the claims. In this case the disclosure is limited to the isolated protox polypeptide of SEQ ID NO:2.

- The lack of guidance and working examples: The claims encompass a vast number of mutant *N. tabacum* protox polypeptides having any structural variation relative to SEQ ID NO:2. The specification provides only a single working example of a method for isolating the polypeptide and encoding nucleic acid of SEQ ID NO:2. The specification fails to provide further guidance for isolating mutants of SEQ ID NO:2 having any structure as encompassed by the claims. Because the claims broadly encompass mutants having any structure, a skilled artisan would readily recognize that the working example, i.e., SEQ ID NO:2, as provided in the specification would not be so useful in isolating other *N. tabacum* protox polypeptides as their encoding sequences may not be sufficiently homologous for identification of other protox isoforms by such methods as hybridization - for example, Lermontova et al. (already of record) teach the presence of two protox isoforms isolated from *N. tabacum* that share only 27% identity. Furthermore, the specification fails to provide a sequence that is conserved throughout protox polypeptides that would be useful in identifying the broad scope of claimed mutant protox polypeptides.

- The high degree of unpredictability in the art: As the structures of the broad scope of claimed mutant protox polypeptides is unlimited, a skilled artisan would recognize the high degree of unpredictability for applying the methods disclosed in the specification with an expectation of obtaining the entire scope of claimed protox polypeptides, particularly in view of the lack of guidance and working examples provided in the specification.

- The amount of experimentation required is undue: While methods of isolating a variant of a given polypeptide, *e.g.,* by hybridization using the encoding nucleic acid as a probe, it is not routine in the art to screen for all mutants of a given polypeptide as broadly encompassed by the claims. Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

It is noted that this rejection has been applied to a claim (claim 2) previously indicated as being allowable with the exception of being dependent upon a rejected base claim. However, upon further review of the specification and upon reconsideration of the scope of the claim, the examiner has determined that the specification fails to enable the full scope of the claim.

Applicants traverse the instant rejection arguing that claim 1 has been amended to limit the scope of mutant protox polypeptides to those that are naturally occurring in

N. tabacum, have the enzyme activity of SEQ ID NO:2, and have tolerance to photobleaching herbicide equivalent to SEQ ID NO:2. Applicants argue the specification teaches methods for isolating and expressing a polynucleotide encoding the claimed mutant protox polypeptide. Applicants argue that in view of the allegedly narrow scope and teachings of the specification, one of skill in the art would be able to make the entire scope of mutant protox polypeptides. Applicants' argument is not found persuasive.

As stated above, the specification fails to provide the necessary guidance for isolating the broad scope of claimed mutant protox polypeptides. The instant case is analogous to *University of Rochester v. G.D. Searle & Co. Inc.,* W.D. N.Y., No. 00-CV-6161L, 3/5/03. The court stated, "although the '850 patent describes an assay for determining whether a given compound possesses certain desired characteristics, and identifies some broad categories of compounds that *might* work, these descriptions, without more precise guidelines, amount to little more than 'a starting point, a direction for further research'". Applicants argue that the specification provides methods for screening plants for a nucleic acid expressing the claimed mutant *N. tabacum* protox polypeptide, creating expression vectors, transforming plants with such vectors, and achieving expression of an encoded polypeptide. As the specification provides no guidance as to a conserved structural feature present in all protox isoforms of *N. tabacum,* one can merely speculate that such mutants *might* be obtained by the methods presented in the specification. The teachings provided by the specification as described above merely provide a starting point for additional research providing no more than a plan or invitation for those of skill in the art to experiment in order that

entire scope of mutant protox polypeptides *might* be isolated. For the reasons stated above, this would clearly require undue experimentation.

Claim Rejections - 35 USC § 102

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

[9] Claim(s) 1-2 and 8 is/are rejected under 35 U.S.C. 102(a) as being anticipated by Lermontova et al. (already of record). Claims 1-2 and 8 are drawn to (in relevant part) an isolated protophorphyringogen oxidase (protox) polypeptide mutant of SEQ ID NO:2 that is naturally occurring in *N. tabacum*, has enzyme activity equivalent to SEQ ID NO:2, and has tolerance to photobleaching herbicide equivalent to SEQ ID NO:2 and optionally wherein the polypeptide has one or more amino acid deletions of SEQ ID NO:2. Lermontova et al. teach a protox polypeptide (NTPPXII) and encoding nucleic acid obtained from *N. tabacum* mitochondria (page 8897, Figure 1). Lermontova et al. teach NTPPXII maintained protox activity in the presence of 100 nM of acifluorfen (page 8899, left column). This anticipates claims 1-2 and 8 as written.

[10] Claim(s) 1-2 and 8 is/are rejected under 35 U.S.C. 102(b) as being anticipated by Ichinose et al. (*J Plant Physiol* 146:693-698). Claims 1-2 and 8 are drawn to (in relevant part) an isolated protophorphyringogen oxidase (protox) polypeptide mutant of SEQ ID NO:2 as described above. Ichinose et al. teach *N. tabacum* cell line YZI-1S, which exhibits a 150-fold increase to the herbicide S23142 (page 697, right column). Ichinose et al. teach that YZI-1S herbicide resistance is due in part to "alteration of the Protox

molecule" (page 697, right column). Ichinose et al. teach, "Protox isolated from YZI-1S cells was more resistant to S23142 inhibition than that of wild-type cells" (page 697, left column and Figure 7). This anticipates claims 1-2 and 8 as written.

It is noted that the claimed mutant protox polypeptide is limited to those that have a tolerance to photobleaching herbicide equivalent to SEQ ID NO:2. Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not have tolerance to photobleaching herbicide equivalent to SEQ ID NO:2). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

[11] In view of applicants' amendment to claims 1 and 8 to limit the claimed mutant polypeptides to those that are naturally occurring in *N. tabacum,* the rejections of claims 1 and 8 under 35 USC 102(b) and 102(e) as being anticipated by Ward et al. and Volrath et al., respectively, are withdrawn. Neither Ward et al. nor Volrath et al. teach a polypeptide having the sequence of SEQ ID NO:2 or a mutant thereof that is naturally occurring in *N. tabacum.*

Conclusion

[12] Status of the claims:

- Claims 1-2, 5, and 8 are pending.
- Claims 1-2 and 8 are rejected.

- Claim 5 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652